PATENT

Attorney Docket No: 3578-120

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re:	Patent application of Radmila Mileusnic, et al	:	
Serial No:	09/998,491	:	Group Art Unit: 1647
Filed:	November 30, 2001	:	
		:	Examiner: Jegatheesan Seharaseyon
For:	POLYPEPTIDES AND THEIR USES	:	Confirmation No: 6361

DECLARATION OF STEVEN PETER RUSSELL ROSE, Ph.D.

I, Steven Peter Russell Rose, Ph.D, declare as follows:

1. I am an inventor, jointly with Radmila Mileusnic, of an invention entitled "Polypeptides and their Uses" which is the subject of US Patent Application 09/998491 (hereinafter "the Application"), filed on 30 November 2001.

2. I am Professor of Biology and Director of the Brain and Behaviour Research Group at The Open University located at Milton Keynes in the UK. I was educated at Cambridge University and was awarded a double first class degree in Biochemistry in 1959. I took a PhD at the Institute of Psychiatry in London in 1961. After periods of postdoctoral research at Oxford (Fellow, New College), Rome (NIH Fellow) and with the Medical Research Council in London I became in 1969 Professor and Chair of the Department of Biology at Britain's newly formed Open University, where I established and have directed ever since the Brain and Behaviour Research Group, focussing my research on understanding the cellular and molecular mechanisms of learning and memory. My research in this area has led to the publication of some 300 research papers and various international honours and medal awards including the Sechenov and Anokhin Medals (Russia) and the Ariens Kappers medal (The Netherlands). In 2002 I was awarded the Biochemical Society medal for excellence in public communication of science, and in 2004 the Edinburgh Medal and Royals Scottish Society of Arts silver medal. During my time at the Open University I have also held visiting professorships and appointments at the Australian National University, Harvard, University of Minnesota (Hill Distinguished Visiting Professor) and the Exploratorium in San Francisco (Osher Fellow).

3. As well as my position at the Open University I was from 1999 to 2002 joint Professor of Physic at Gresham College London (a post held jointly with Professor

Hilary Rose, with a remit to lecture on Œgenetics and society.). I am also a Visiting Professor in the Department of Anatomy and Developmental Biology at University College London. As well as my research papers in neuroscience and related fields I have written or edited 15 books, including two about chemical and biological weapons. My first ever book, written in 1964, The Chemistry of Life, became a minor classic over four further editions, the last being in 1999. Amongst my other authored books have been Science and Society (with Hilary Rose, Penguin, 1969); The Conscious Brain (Weidenfeld, Penguin, Knopf, Vintage and Paragon House reprint, 1973 and later editions); No Fire no Thunder (an account of chemical and biological weapons, with Sean Murphy and Alastair Hay, Pluto, 1984); Not in our Genes (with Richard Lewontin and Leo Kamin; Penguin and Pantheon, 1984); Molecules and Minds (Open University Press, 1989); and more recently The Making of Memory (Bantam UK, 1992 and in the US, Doubleday, 1993), winner of the 1993 Rhone-Poulenc/Royal Society Science Book Prize. All have been translated into a variety of other European languages. Lifelines, was published by Penguin and Oxford University Press in September 1997, (paperback in September 1998). A book on the brain for children, coauthored with a 12 year old, Alexander Lichtenfels, and called Brainbox was also published in 1998 An edited book, From Brains to Consciousness appeared in June 1998, and most recently, edited jointly with Hilary Rose, Alas Poor Darwin: arguments against evolutionary psychology (Cape, July 2000). My latest book is The 21st Century Brain: explaining mending and manipulating the mind, published in March 2005 by Cape. I am editor of the series Maps of the Mind for Weidenfeld and Nicolson.

4. I am a frequent writer and reviewer for newspapers and magazines such as The Guardian, Prospect, The Lancet and New Scientist. I was co-convenor of the Science Engineering and Technology Policy Forum, set up to advise the UK Labour party on science, engineering and technology policy issues prior to the 1997 election. I have been a Council member of the Research Defence Society and a member of COPUS, the Committee on the Public Understanding of Science. I was the 1996 President of the Biology Section of the British Association for the Advancement of Science and have been a Director of the Edinburgh International Science Festival. I am a frequent national and international lecturer, and also have wide experience of radio and television in the context of interviews, discussion, debate and science programmes. I am currently a regular panel member of the British Broadcasting Corporation's Radio 4's The Moral Maze.

5. The claims presently pending in the application include claim 10 which, in its current form, reads as follows:

"A pharmaceutical composition comprising a polypeptide wherein the polypeptide consists of the following sequence of amino acids

Arg-Glu-Arg (SEQ ID No: 9)

and a pharmaceutically acceptable carrier, filler or excipient".

6. In an office action dated 27 October 2005, the examiner has rejected claim 10 as being anticipated by the disclosure of WO-A-94/09808 ("Saitoh"). I understand the essence of the examiner's rejection to be that, although the examiner accepts that Saitoh teaches that the polypeptide of claim 10 (also known as "RER") is biologically inactive (see Saitoh at page 18, lines 7 and 26), Saitoh nevertheless discloses a composition which contains RER and a substance which constitutes "a pharmaceutically acceptable carrier, filler or excipient" within the meaning of that expression in claim 10 above.

7. I am familiar with the disclosure of Saitoh, having long known of the existence and teaching of the document. On studying the document anew in the light of the examiner's objection, it seems to me that the only substance which the examiner could consider to constitute "a pharmaceutically acceptable carrier, filler or excipient" as in claim 10 is the substance "DMEM" which is mentioned at page 16, line 35 of Saitoh. This mention occurs in Example V of Saitoh in which the use of a growth assay to screen a number of peptides (including RER) for activity is described, the peptides having been synthesised in accordance with Example II of Saitoh. In the case of RER, as I have already mentioned, no activity was found.

8. The essential question raised by the examiner's objection therefore seems to me to be:

"Does DMEM constitute a pharmaceutically acceptable carrier, filler or excipient?"

9. DMEM stands for Dulbecco's Modified Eagle's Medium (Saitoh: pages 13, line 1). DMEM is a liquid growth medium for cell cultures. A typical medium contains (in mM) the following constituents.

Glycine	0.400
L-Arginine hydrochloride	0.398
L-Cystine 2HCl	0.201
L-Glutamine	4.00
L-Histidine hydrochloride-H_20	0.200
L-Isoleucine	0.802
L-Leucine	0.802
L-Lysine hydrochloride	0.798
L-Methionine	0.201
L-Phenylalanine	0.400
L-Serine	0.400
L-Threonine	0.798
L-Tryptophan	0.0784
L-Tyrosine disodium salt dihydrate	0.398
L-Valine	0.803
Choline chloride	0.0286
D-Calcium pantothenate	0.00839

Folic Acid	0.00907
i-Inositol	0.0400
Niacinamide	0.0328
Pyridoxine hydrochloride	0.0196
Riboflavin	0.00106
Thiamine hydrochloride	0.0119
Calcium Chloride ($CaCl_2$) (anhyd.)	1.80
Ferric Nitrate ($Fe(NO_3)_3 9H_20$)	0.000248
Magnesium Sulfate ($MgSO_4$) (anhyd.)	0.814
Potassium Chloride (KCl)	5.33
Sodium Bicarbonate ($NaHCO_3$)	44.05
Sodium Chloride (NaCl)	81.90
Sodium Phosphate monobasic (NaH_2PO_4-H_2O)	0.906
D-Glucose (Dextrose)	25.00
HEPES	25.03
Phenol Red	0.0399

This information is taken from the website of Invitrogen Corporation www.invitrogen.com. A copy of the source of the information is exhibited hereto as Exhibit SPRR1.

10. I know from my research activities over the past 43 years, referred to in paragraph 1 above, that DMEM is a typical enriched and buffered tissue culture medium. As such, DMEM is totally unsuitable for use as any carrier, excipient or filler which would be suitable for pharmaceutical administration. I point in particular to the presence of 0.0399 mM of phenol red in the above composition. Thus, a liquid formulation containing 0.0399mM concentration of phenol red would be hazardous or even toxic to humans, if taken either orally or parenterally.

11. In my view therefore, and speaking with the benefit of my experience in the field of biological research going back over the past 43 years, Saitoh does not disclose any composition falling within the scope of my claim 10. Saitoh moreover teaches that RER is biologically inactive and therefore teaches away from claim 10 and my invention.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Steven Peter Russell Rose

22 April 2006

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Serial No:	09/998,491	:	Group Art Unit: 1647
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This is Exhibit SPRR1 referred to in paragraph 9 of my declaration in these proceedings dated 22 April 2006

Steven Peter Russell Rose

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

BY Jennifer P. Hanna

DATE 4/25/06

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Technical Resources - Media Formulations

Dulbecco's Modified Eagle Medium (D-MEM) (1X) liquid (high glucose)
Contains 4500 mg/L D-glucose, L-glutamine and 25 mM HEPES buffer but no sodium pyruvate.

Dulbecco's Modified Eagle Media are well suited for supporting the growth of a broad spectrum of mammalian cell lines.

Catalog Number: 12430047, 12430054, 12430062,

COMPONENTS	Molecular Weight	Concentration (mg/L)	Molarity (mM)
Amino Acids			
Glycine	75	30	0.400
L-Arginine hydrochloride	211	84	0.398
L-Cystine 2HCl	313	63	0.201
L-Glutamine	146	584	4.00
L-Histidine hydrochloride-H2O	210	42	0.200
L-Isoleucine	131	105	0.802
L-Leucine	131	105	0.802
L-Lysine hydrochloride	183	146	0.798
L-Methionine	149	30	0.201
L-Phenylalanine	165	66	0.400
L-Serine	105	42	0.400
L-Threonine	119	95	0.798
L-Tryptophan	204	16	0.0784
L-Tyrosine disodium salt dihydrate	261	104	0.398
L-Valine	117	94	0.803
Vitamins			
Choline chloride	140	4	0.0286
D-Calcium pantothenate	477	4	0.00839
Folic Acid	441	4	0.00907
i-Inositol	180	7.2	0.0400
Niacinamide	122	4	0.0328
Pyridoxine hydrochloride	204	4	0.0196
Riboflavin	376	0.4	0.00106

Thiamine hydrochloride	337	4	0.0119
Inorganic Salts			
Calcium Chloride (CaCl2) (anhyd.)	111	200	1.80
Ferric Nitrate (Fe(NO3)3 9H2O)	404	0.1	0.000248
Magnesium Sulfate (MgSO4) (anhyd.)	120	97.67	0.814
Potassium Chloride (KCl)	75	400	5.33
Sodium Bicarbonate (NaHCO3)	84	3700	44.05
Sodium Chloride (NaCl)	58	4750	81.90
Sodium Phosphate monobasic (NaH2PO4-H2O)	138	125	0.906
Other Components			
D-Glucose (Dextrose)	180	4500	25.00
HEPES	238	5958	25.03
Phenol Red	376.4	15	0.0399

***Note:** Pyridoxine HCl replaces pyridoxal HCl.

REFERENCE:

1. Dulbecco, R. and Freeman, G. (1959) Virology 8:396.